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DISPOSABLE PIEZOELECTRIC CRYSTAL MICROBALANCE FLOW CELL

The present invention relates to a disposable pre-coated piezoelectric crystal microbalance flow cell, and a method of detecting an analyte in a fluid by use of the flow cell in a sensor system.

BACKGROUND

The principle of detecting a chemical by measuring a change in the sensor mass in response to the interaction of a surface of the sensor with a solution containing the chemical is known, for example, from US patent No. 5,705,399 (Larue). By analysis, the piezoelectric crystal is normally placed in a cell that delivers the sample liquid onto the piezoelectric sensor surface. The crystal, and sometimes also the cell, has to be regenerated for multiple use. This is time-consuming and less practical, especially for screening purposes. It would be advantageous to have a disposable pre-coated piezoelectric crystal mounted in a flow cell for screening of a large number of samples. When the sensor surface is inactive after use, the whole flow cell can be replaced.

DESCRIPTION OF THE INVENTION

The invention provides a rugged, disposable self-contained flow cell comprising a coated piezoelectric crystal prepared for instant use by plugg-in to a connector station capable of providing a flow of fluid in and out of a compartment of the cell as well as oscillation of the crystal by connection to an oscillation unit and signal processing electronics for detection of mass change on the crystal when analyte(s) interacting with the coating is(are) present in the flow.

According to one aspect of the present invention there is provided a disposable piezoelectric crystal microbalance flow cell comprising:

a sealed cell housing having external fluid and electric connector means for interfacing with external solution flow, electric power and electronic control equipment upon detachably connecting said flow cell to a connecting station of a sensor system, said electronic control equipment being designed for detecting a deviation from oscillating characteristics, such as serial capacitance, Q-value and resonance frequencies, of an oscillating piezoelectric sensor crystal in said housing in response to said crystal changing its mass,

said sensor crystal comprising a first face and a second opposite face, each having a respective metal electrode for oscillating said sensor crystal, and having a pair of contact patches for electrically connecting said electrodes to said station via said connector

means, the metal surface of the electrode on said first face being the metal surface having a coating; and

isolating means for fluidly isolating a compartment comprising the coating in the cell from said contact patches, said fluid compartment being adapted for fluid communication with said station via connector ports of said connector means.

The change in mass on the sensor crystal will normally depend on a change in the composition of the coating on either or both sides of the sensor crystal.

Depending on the desired reaction to occur and to be detected, the coating on the sensor crystal is pre-selected and provided in the flow cell of the invention. In addition to a coating on the sensor crystal, there may be provided additional coatings and/or reaction components and/or stabilizers and/or auxiliary components in the flow cell, selected for each specific need and/or customer desire.

Examples of detectable changing in mass on the sensor crystal is as a result of interaction between a first member of an interaction pair attached to the coating on a metal surface of the sensor crystal and a second member of the interaction pair present in a fluid.

The fluidly isolated compartment may comprise the first member of the interaction pair separated from the coating on the metal surface for activation of the coating with the first member prior to use. This may improve the shelf life of the flow cell in dry state and the sensitivity in the analysis of analyte. When the flow cell is to be used for analyte detection, a solution is passed through the dry cell thereby releasing the first member of the interaction pair from its position separated from the coating. The first member can be stored in the inlet tube, the walls, the ceiling or a separate compartment in the cell. The first member can be in a dry state or wet state. The free first member is then reversibly activating the coating, which comprises a chemical derivative of the second interaction member with a lower affinity to the first interaction member than the analyte being the second member of the interaction pair, and the flow cell is thereby activated for use in detecting a specific analyte in a fluid.

A special embodiment of the present invention is when the coating exposing the first member of the interaction pair is situated at a distance from the electrodes and the first member is reversibly bound to the coating. When a second member of an interaction pair is present in a fluid, the first member is displaced from the coating as it interacts with the second member to form the interaction pair. This interaction pair is displaced from the surface, subsequently attracted and adsorbed by a second coating on the electrode, thus resulting in a

measurable mass enhancement on the electrode, measured by a decrease of the frequency and Q-value.

In a presently preferred embodiment of this special embodiment of the invention, the second coating that is situated on one or both of the electrodes is e.g. a protein that attracts and adsorbs an antibody-antigen complex. Examples of such proteins are Protein A and G.

Preferably the first member of the interaction pair is an antibody reversibly bound to the coating, especially an antibody specifically binding to an explosive, such as one selected from the group consisting of trinitrotoluene (TNT), dinitrotoluene (DNT), hexahydro-1,3,5-trinitro-1,3,5-triazine (RDX), octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazine (HMX), pentaerythritol tetranitrate (PETN), and nitroglycerine (NG), or a narcotic, such as one selected from the group consisting of cocaine, heroine, amphetamine, methamphetamine, cannabinols, tetrahydrocannabinols (THC), and methylenedioxy-N-methylamphetamine (ecstacy).

The coating on the piezoelectric crystal may comprise two or more different attached first members of interaction pairs. With this embodiment of the flow cell screening of the occurrence of any of a number of analytes, such as several narcotics or explosives, can be made at the same time. This is also the case when the coating is divided into two or more discrete patches on the metal electrode each comprising different attached chemically modified derivatives of the first members of interaction pairs.

The fluid cell according to the invention may be part of an array unit comprising two or more fluid cells according to the invention. Such an array unit can be used in a multicell-flowthrough sensor system. The fluid cell according to the invention may also contain one or several electrodes on one crystal or several crystals having one or several electrodes.

According to another aspect of the invention there is provided a method of detecting an analyte in a fluid by using a sensor system, comprising oscillating a piezoelectric crystal in a flow cell according to the invention in a fluid, wherein the coating on the metal of the piezoelectric crystal electrode attracts, reversibly or irreversibly, a first member of an interaction pair, stabilizing the oscillating characteristics of the piezoelectric crystal at a constant flow rate of fluid lacking analyte, introducing a fluid sample containing an analyte being a second member of the interaction pair to the flow cell at the same constant flow rate, and detecting change of mass on the coating on the piezoelectric crystal electrode as a change

in oscillating characteristics resulting from interaction between the first member and the second member of the interaction pair.

In a presently preferred embodiment the piezoelectric crystal electrode positioned in the piezoelectric crystal microbalance flow cell of the invention comprises a metal surface, on either or both sides of the crystal, which is coated with a coating comprising one member of an interaction pair. The other member of the interaction pair is an analyte to be detected in an aqueous solution.

The metal of the surface is preferably selected from the group consisting of gold, silver, aluminum, nickel, chrome and titanium. The crystal of the piezoelectric electrode is e.g. a frequently used quartz crystal, an aluminum nitride (AlN) crystal or a sodium potassium niobiates (NKN) crystal.

Examples of interaction pairs that can be detected in the present invention include anions-cations, antibodies-antigens, receptor-ligand, enzyme-substrate, oligonucleotide-oligonucleotide with complementary sequence, oligonucleotide-protein, oligonucleotide-cell, and peptide nucleic acid (PNA) oligomer - polynucleotide, wherein the polynucleotide may be selected from the group consisting of RNA, DNA and PNA polymers complementary to the PNA oligomer.

Upon exposure to the analyte in a fluid, the coating on the metal surface of the piezoelectric crystal will interact with the analyte, either increasing the mass of the coating by attachment of the analyte or the interaction pair, or decreasing the mass of the coating by displacement of the first interaction partner form the coating. This change of mass on the coated metal surface of the electrode is detected by the piezoelectric crystal microbalance sensor and indicates presence of the analyte in the fluid.

The invention can also be utilized with cells comprising electrodes that have two or more different first members of interaction pairs for detection of at least one of the corresponding second member analytes. The electrodes may also comprise only one first interaction member for ensuring detection of just one analyte of interest.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1a is a diagrammatic view of a sensor system incorporating cells according to the invention in a sample loading state of the loop

Fig. 1b is a diagrammatic view of a modified sensor system in a solution flowing state;

Fig. 2 is a view showing a connecting face of a sensor cell according to the invention;

Fig. 3 is a view showing a face of a sensor cell opposite to that of Fig. 2;

Fig. 4 is an inside plan view of the upper cell half shown in Fig. 2;

Fig. 5 is a plan view of a sensor crystal according to the invention;

Fig. 6 is a fragmentary view, partly in section along plane 6 of Fig. 2;

Fig. 7 is another view showing a sensor crystal according to the invention;

Fig. 8 is a plan view of a connecting station according to the invention;

Fig. 9 is a plan view of a connecting station of Fig. 8 receiving a battery of cells;

Fig. 10 is a diagram showing the individual response of two serially coupled sensor cells; and

Fig. 11 is another diagram showing the individual response of two serially coupled sensor cells.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

A preferred embodiment of a sensor device comprising a disposable piezoelectric microbalance cell 10 according to the invention is shown in Figs. 2 and 3. The cell 10 has a housing 12 assembled by a pair of injection-molded halves 14, 16 of polymeric material. The halves 14, 16 are permanently sealed.

The cell does not need to have a square or cornered shape as shown but may suitably take other shapes such as circular or oval (not shown).

A rear face 20 of the housing 12 has a central connector portion 24 for connection to an electric power and electronic control equipment , i.e. power and measurement unit 130, and to a solution flowing unit 70 (Fig. 1a) to be later described. The front face 22 of the housing is preferably provided with an identification marking or label 23.

The connector portion 24 has a pair of electric connector ports 26 and 28 flush with the rear face 20 and a pair of fluid connector ports 30 and 32 projecting from the rear face 20. The connector ports 26, 28, 30 and 32 of a cell 10 are adapted for operative engagement with respective complementary shaped connector ports 122, 124, 126, 128 of each of a plurality of cell receptors or connecting sockets 118 (Fig. 8) at a connecting station100 when the cell 10 is plugged into the socket.

In the embodiment shown in Fig. 2 and 4 and, the electric connector ports 26 and 28 comprise through-bores in the cell half 14. The ports 26, 28 enter a closed cavity 38 in the cell half 14 of housing 12 in alignment with respective connector patches 58, 64 of a sensor crystal 50 to be later described received in cavity 38. When the cell 10 is detachably docked to the station 100 or 101, electric contact pins 114, 116 (Fig. 6) located in the ports 26,

28 contact the respective contact patches 58, 64 and are electrically connected to the power and measurement unit 130 via the connecting station 100 or 101. The externally projecting pins 114, 116 may be permanently secured, optionally to the connecting station 100 as indicated in Fig. 1a, or to the cell 10 as indicated by phantom lines in Fig. 2. The pins 114, 116 can further be axially spring-loaded in a direction to securely contact the patches 58, 64. Other means of secure electrical contact to patches 58, 64 are possible. For example, the ports 26,28 may be provided with conventional female conducting sockets (not shown) that are made to contact the patches when the halves 14, 16 are assembled. In the preferred embodiment, however, the contacting pins 114, 116 are made easily interchangeable in order to eliminate decrease in performance due to wearing of the electrical contacting surfaces.

In the embodiment shown in Fig. 2, 4 and 6, the fluid connector ports 30 and 32 also comprise through-bores in the cell half 14. Ports 30, 32 enter a closed, small volume (a few μl) circular compartment 34 in cell half 14 of housing 12. A central portion of sensor crystal 50, an opposite wall 36 of the cavity 38 and an O-ring sealing 68 interposed there between, defines the compartment 34. Compartment 34 is thereby fluidly isolated in the cavity 38 and prevents solution and test solution to reach the contact patches 58, 64. This arrangement allows the solution to be flowed through the compartment 34 via the connector ports 30, 32 in the direction indicated by the arrows in Fig. 6.

The sensor crystal 50 (Fig. 7) is a piezoelectric resonant quartz crystal 52, for example a high Q-value 10 MHz quartz crystal, having deposited on its opposite faces 54 and 60 respective electrodes 56 and 62. By respective conductive paths 57, 63, each electrode 56, 62 is electrically connected to the respective contact patch 58, 64 located on the common face 54 of crystal 52.

By applying AC voltage to the electrodes 56, 62 the crystal 50 will oscillate in a shear mode wave, at a certain resonance frequency. The resonance frequency of the crystal is dependent on the crystal material (for example AT-cut quartz), its thickness, crystal surface coating (electrodes and chemical coating), surrounding medium viscosity, electromagnetic disturbances, electrostatic disturbances as well as temperature and pressure. The principle of detection is to stabilize the crystal oscillation from all the above parameters except for the chemical coating, which can then be monitored in a relative sense by logging of the resonance frequency in the power and measurement unit 130.

In the embodiment of Fig. 6, a backing plate 40 supports the opposite face 60 of the crystal 50 mounted in the cavity 38. To allow the crystal 50 to oscillate as freely as possible in compartment 34, backing plate 40 has a peripheral rim or flange 42 defining a

hollow space 44 opposite to the compartment 34. In a preferred embodiment, an alternative rim or flange 43 extends radially outwards to the edges of crystal 50 to eliminate mechanical stress from the contact pins 114, 116 by support on the opposite face 60 of crystal. The support may alternatively be restricted to portions opposite the contact pins 114, 116 (not shown). In certain applications, to improve the resonant properties of the crystal, the isolated space 44 may possibly be filled with a viscous fluid. By appropriate dimensioning, this closed design of the cell 10 will mechanically define the applied clamping pressure on the crystal 50, thereby eliminating variation in performance between sensors due to operator dependence.

The electrode 56 facing the compartment 34 is coated with a coating 66. Generally, the coating 66 is adapted to interact, chemically or biochemically, exclusively with a matching particular chemical or analyte possibly present in the solution 83 resulting in a slight change, increase or decrease, of mass of the crystals. In another embodiment, the opposite wall 36 in the compartment 34 is coated with a complementary or paired coating 46 to supplement the coating 66 as a member of a two-component system in order to activate the cell 10 when exposed to the solution 83. In still another embodiment, the electrode 66 is coated by at least one additional coating 67 (Fig. 6) that, in turn, optionally can also have a complementary separate coating (not shown) in the compartment 34. By such alternative arrangements of multiple or paired coatings, a single cell 10 will be able to detect more than one particular chemical.

The change of mass will slightly alter the oscillating characteristics of the crystal 50, which is detected by a computerized evaluation process in the power and measurement unit 130.

In operation, when each of one or more cells 10 is plugged into a connecting socket 118 of the connecting station 100 (Fig. 1a and Fig.8), the crystal 50, electrically connected to the power and measurement unit 130, is oscillated at its resonant frequency. At the same time, a plug of solution, i.e. a volume of aqueous solution trapped between volumes of a solution 75 in fine caliber tubing, flows from the flowing station 70, through the connecting station 100 and enters the compartment 34 in the cell 10. The solution 75, which can be an aqueous solution identical to the solution 83, has the function of transporting the plug of the solution 83 to the cells 10.

Accordingly, if an analyte matching the coating or coatings in the cell compartment 34 is present in the solution 83, the coating(s) will interact with the analyte, and the crystal 50 will change oscillating characteristics, such as resonant frequency, which is detected and signaled by the power and measurement unit 130 for further use.

As shown in Fig. 8, the connecting station 100 is comprised of a connecting rack or panel 112 having a plurality of connecting receptors or sockets 118 for docking a corresponding number of cells 10. Each socket 118 may be shaped as a depression in the panel front and may have a dent 120 to mate with an indent 18 of the cell 10 to prevent improper orientation on insertion of cell 10 in socket 118.

As shown in Fig. 1a, in the preferred embodiment, the sockets 118 of the connecting station 100 are serially connected to the flowing unit 70 in a manifold. More precisely, an inlet flow line 98 to the connecting station 100 will be connected to the inlet port 32 of a cell 10 in the first socket 118, and line segments 102 between each consecutive cell 10 plugged into the station 100 will connect the outlet port 30 of a previous cell 10 with inlet port 32 of the following cell 10. The outlet port of the last cell 10 is connected to a waste reservoir 106 through an outlet line 104. To avoid electric interference between cells 10 caused by the electrically conducting solution 83, the solution 83 flowing in inlet line 98 and line segments 102 is electrically grounded by grounding conductors 108. To further avoid electric interference including electromagnetic and electrostatic disturbances, the cells 10 are totally enclosed by an electric shield 109, for example a metal casing, as schematically shown in phantom in Fig. 3. Preferably, other components of the system are also shielded

In order to further eliminate cell-to-cell interference, the driving electronics of the power and measurement unit 130 is tuned such that the liquid or flow side of the crystal 50 is at ground potential.

An alternative parallel flow connecting station 101 having a panel 113 for parallel connection of the cells 10 to the flowing unit is diagrammatically shown in Fig. 1b.

While the connecting station 100 may be provided with valve means for automatically shutting off the flow to unused sockets 118 and direct it to the waste reservoir 106, in the preferred embodiment all sockets of the panel 112 should be plugged with cells 10. If by any reason all sockets are not intended to be occupied with functional cells 10 having different coatings for the detection of different chemicals, dummy cells 10' (Fig. 8) having no coatings and crystals but only the compartment and ports (not shown) for passing the flow further, may be used to occupy all unused sockets and direct the flow to the reservoir 106.

In the embodiment of Fig. 9, there is shown a battery 11 of multiple cells 10 in a common housing adapted to occupy all sockets 118 and having mutually different coatings (not shown) on the electrodes 50 and/or compartment walls. Optionally, one or more cells 10 in the battery 11 may also be dummy cells 10', as desired.

Returning to Fig. 1a, the flowing unit 70 is composed of a fluid distributing system including fine caliber tubing and valves having small dead volumes to handle the usually small volumes of solution 83 that are obtained, for example by condensation of an evaporated volume of air that may contain the analyte to be detected by the system of the invention. Example of tubing is standard HPLC PEEK or stainless steel tubing having an inner diameter of 0.25 mm to achieve acceptable sample dispersion and yet not too large pressure loss in the system.

The flowing unit 70 is designed and adapted to operate as follows:

A valve arrangement comprising valves 86 for loading and introducing the plug of solution between ends of the solution 75 is shown in two different positions in Fig. 1a and Fig. 1b. While other valve arrangements are conceivable to fulfill the desired functions, the valve arrangement 86 according to the invention operates as follows:

In the first position shown in Fig. 1a, valve 86 allows introducing the solution 83 to a loop 90 of tubing from an injector 82 via a line 84 to form the plug of solution. At this stage, valve 86 directs loop 90 to a waste line 96 until the injection of the plug of solution 83 is completed so that a portion of the solution 75 in front of the plug in loop 90 is received by a waste reservoir 94.

In the second valve position, the plug of test solution 83 is now trapped between volumes of solution 75. Valve 86 connects loop 90 to line 98. By continuing action of pump 76 the plug of test solution in the loop 90 will now be introduced to the connecting station 100 and to the compartments 34 (Fig. 6) of the cells connected to the panel 112 such that the analyte(s) possibly present in the flow will interact with the coatings. At this moment, also the power and measurement unit 130 starts the detection process as described.

It is very important that the flow through the cell compartments 34 has a steady flow with little or no pulsations in order not to affect the oscillating characteristics, such as resonant frequency, of the crystal. The pump 76, for instance a peristaltic pump, should therefore have a minimum of pulsations. The pump is preferably a low flow rate (5-500µl/min), low pressure pump delivering a stable flow pressure and flow rate. An important component of the feeding unit 72 is a pulse dampener 80, which stabilizes the flow and reduces pulses from the pump 76 as well as eliminates air bubbles in the flow. The pulse dampener 80 comprises a partially filled closed container (volume about 2ml) for accumulating a volume of the flowing solution 75 together with a possibly pressurized compressible fluid.

In the second valve position, the plug of test solution 83 is now trapped between volumes of solution 75. Valve 92 connects loop 90 to line 98. By continuing action of pump 76 the plug of solution in the loop 90 will now be flowed to the connecting station 100 and flow the compartments 34 (Fig. 6) of the cells connected to the panel 112 such that the analyte possibly present in the flow will interact with the coatings. At this moment, also the power and measurement unit 130 starts the detection process as described.

EXAMPLE

An analysis system was prepared by surface coating of the crystals with their respective antigensone for each different substance to detect. Each antigen has a weaker affinity to an antibody than the substance to be detected. The coated crystals were inserted into the cell housing and thereafter docked to the flowing system. The pump was turned on and the pulse dampener was filled with solution to half its volume. The system was allowed to stabilize during ten to 30 minutes, until the frequency baselines had a drift below 2 Hz/min and a noise level below 1 Hz.

Antibodies (AB) of 0.02 g/l against the substances to be detected (analytes) and the coating antigens were injected into the system with the 100 µl loop. A negative frequency shifts of 50 to 200 Hz of the crystals were observed at their respective AB-injection (see Figs 10 and 11). When the antibodies have been loaded onto the antigen-containing coating on the metal surfaces, the system is ready for detection. A sample, containing two or more of the substances (concentrations 10-1000 pg/µl) were injected via the sample loop. As can be seen in Figure 10 and 11 the crystals with the corresponding antibodies received a positive frequency shift of 5-50 Hz depending on the injected concentration.

Fig. 10 shows the individual response of two serially connected sensor cells. Cell No. 1 is an amphetamine cell and reacts on samples containing amphetamine but not TNT. Cell No.2 is a TNT cell and reacts only at the presence of TNT but not amphetamine.

Fig. 11 corresponds to Fig. 10 but is reversed. Cell No. 1 is a TNT cell and Cell No.2 is an amphetamine cell.

The relevant data in the detection of amphetamine and TNT using a series flow cell system based on QCM (Quartz Crystal Microbalance) technology were as follows:

Flow rate:	100 µL/min
Injection volume:	100 µL
Rubber gasket (O-ring):	Viton 5.8

Antigen fc1 (Fig. 11): TNT PAG25

Antigen fc2 (Fig. 11): Amphetamine B002

Abbreviations:

PBS	Phosphate saline buffer pH 7.4
TNT	Trinitrotoluene
APH	Amphetamine
ABTNT	Antibodies with specificity for TNT
ABAPH	Antibodies with specificity for Amphetamine

The concentrations of ABTNT and ABAPH were 0.02 g/L. The concentrations of TNT and amphetamine are given in pg/μL. The running buffer was PBS pH 7.4.

CLAIMS

1. A disposable piezoelectric crystal microbalance flow cell (10) comprising:

a sealed cell housing (12) having external fluid and electric connector means (24) for interfacing with external solution flow, electric power and electronic control equipment (70, 130) on detachably connecting said flow cell (10) to a connecting station (100,101) of a sensor system, said electronic control equipment being designed for detecting a deviation from oscillating characteristics of an oscillating piezoelectric sensor crystal (50) in said housing (12) in response to said crystal changing its mass,

said sensor crystal (50) comprising a first face and a second opposite face, each having a respective metal electrode (56, 62) for oscillating said sensor crystal (50), and having a pair of contact patches (58, 64) for electrically connecting said electrodes (56, 62) to said station (100,101) via said connector means (24), the metal surface of the electrode on said first face (56) being the metal surface having a coating (66); and

isolating means (68) for fluidly isolating a compartment (34) comprising the coating (66) in the cell from said contact patches (58, 64), said fluid compartment (34) being adapted for fluid communication with said station (100,101) via connector ports (32, 30) of said connector means (24).

2. The flow cell according to claim 1, wherein the changing of mass of the crystal is a result of an interaction between a first member of an interaction pair attached to the coating (66) on the metal surface of the sensor crystal (50) and a second member of the interaction pair present in a fluid.

3. The flow cell according to claim 1, wherein said fluidly isolated compartment (34) comprises a first member of the interaction pair (38) separated from the coating on the metal surface (66) for activation of the coating with the first member prior to use.

4. The flow cell according to claim 1, wherein at a distance from the electrodes (56, 62), one of which contains the coating (66), is situated another coating (46) exposing a first member of an interaction pair, and the first member is reversibly bound to that coating (46) in solution, and in use, a second member of the interaction pair is present in a fluid, the first member is displaced from its coating (46) as it interacts with the second member to form the interaction pair, which is subsequently attracted and adsorbed by the coating (66) on the electrode resulting in a measurable mass enhancement on the electrode.

5. The flow cell according to claim 2 or 3, wherein said first member of the interaction pair is an antibody reversibly bound to the coating (66).

6. The flow cell according to claim 5, wherein said antibody is an antibody specifically binding to an explosive or a narcotic.

7. The flow cell according to claim 6, wherein the explosive is selected from the group consisting of trinitrotoluene (TNT), dinitrotoluene (DNT), hexahydro-1,3,5-trinitro-1,3,5-triazine (RDX), octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazine (HMX), pentaerythritol tetranitrate (PETN), and nitroglycerine (NG).

8. The flow cell according to claim 6, wherein the narcotic is selected from the group consisting of cocaine, heroine, amphetamine, methamphetamine, cannabinols, tetrahydrocannabinols (THC), and methylenedioxy-N-methylamphetamine (ecstacy).

9. The flow cell according to any one of the claims 1 – 8, wherein the coating comprises two or more different attached first members of interaction pairs.

10. The flow cell according to any one of claims 1 – 8, wherein the coating is divided into two or more discrete patches each comprising different attached first members of interaction pairs.

11. The flow cell according to any one of the preceding claims, as part of an array unit (112) of said connecting station comprising two or more flow cells according to any one of claims 1 – 9.

12. The flow cell according to any of the preceding claims, wherein said connector means (24) is adapted for mating engagement with a connector portion (120) of the connecting station (100).

13. The flow cell according to any of the preceding claims, further comprising support means (42; 43) for supporting said second face (60) of the crystal (50).

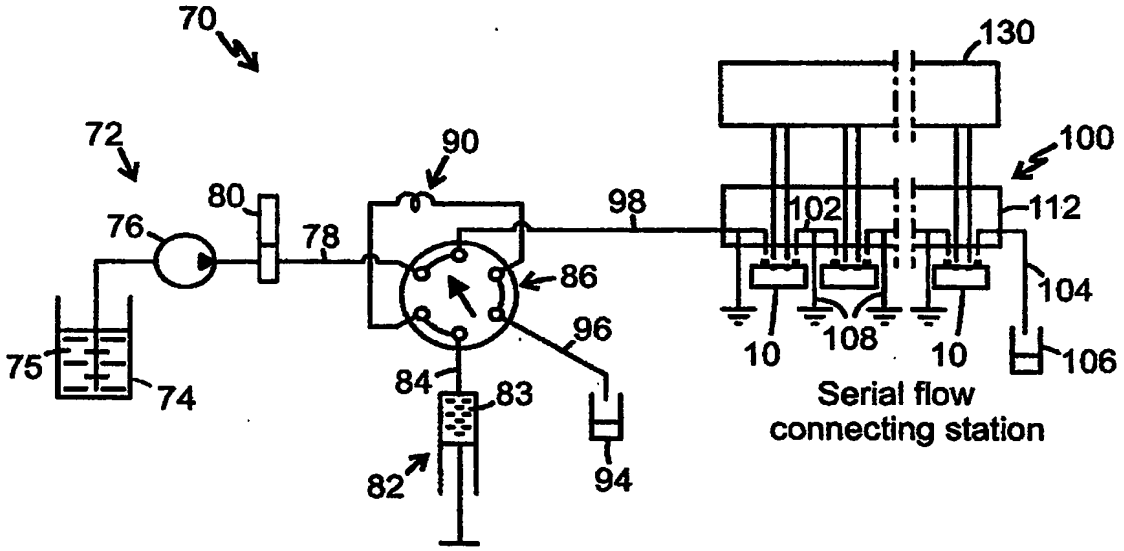
14. The flow cell according to any of the preceding claims, further comprising an electrical shield (109) enclosing the cell (10).

15. A method of detecting an analyte in a fluid by using a sensor system, comprising oscillating a piezoelectric crystal in a flow cell according to any one of the preceding claims in a fluid, wherein the coating on the metal of the piezoelectric crystal electrode attracts, reversibly or irreversibly, a first member of an interaction pair, stabilizing the oscillating characteristics of the piezoelectric crystal at a constant flow rate of fluid lacking analyte, introducing a fluid sample containing an analyte being a second member of the interaction pair to the flow cell at the same constant flow rate, and detecting change of mass on the coating on the piezoelectric crystal electrode as a change in oscillating characteristics resulting from interaction between the first member and the second member of the interaction pair.

ABSTRACT

A disposable piezoelectric crystal microbalance flow cell (10) and its use are described. The flow cell (10) comprises a sealed cell housing (12) having external fluid and electric connector means (24) for interfacing with external solution flow, electric power and electronic control equipment (70, 130) on detachably connecting said flow cell (10) to a connecting station (100,101) of a sensor system. The flow cell (10) further comprises a sensor crystal (50) having metal electrodes (56, 62) for oscillating the sensor crystal (50), and having a pair of contact patches (58, 64) for electrically connecting said electrodes (56, 62) to the station (100,101) via the connector means (24), and isolating means (68) for fluidly isolating a compartment (34) comprising a coating (66) on the electrode (56,62) in the cell from said contact patches (58, 64), said fluid compartment (34) being adapted for fluid communication with said station (100,101) via connector ports (32, 30) of said connector means (24).

(Fig. 4)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72
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98
130
100
102
112
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106
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83
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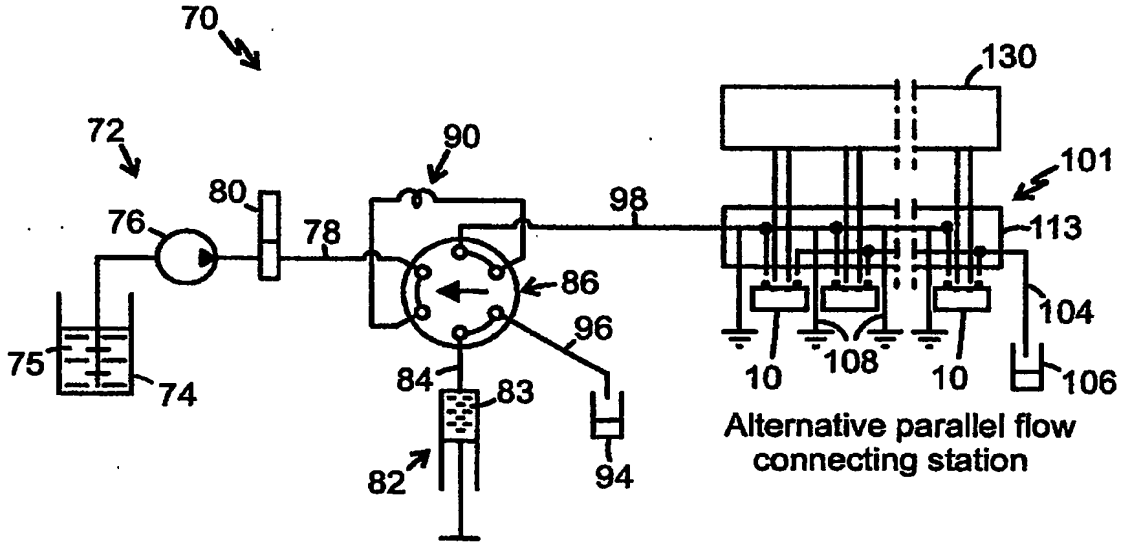
94
10
108
10
Serial flow
connecting station

Fig.1a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90
98
130
101
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75
74
84
83
82
94
10
108
10
Alternative parallel flow
connecting station

Fig.1b

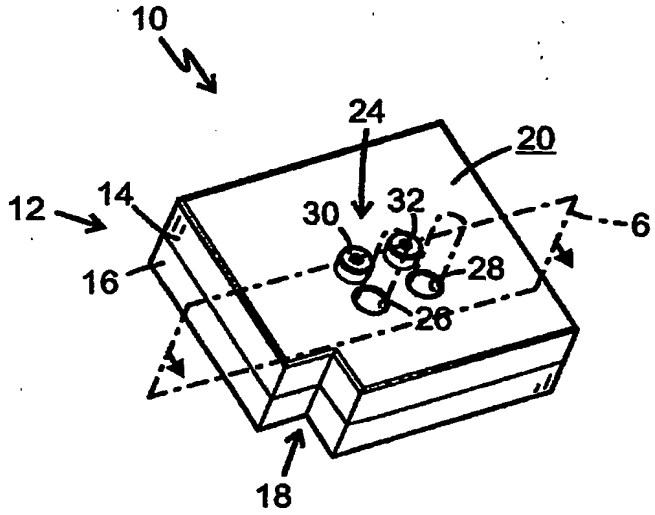


Fig. 2

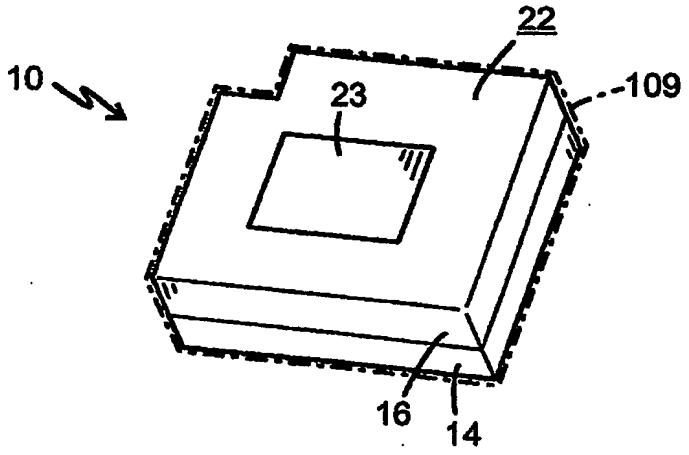


Fig. 3

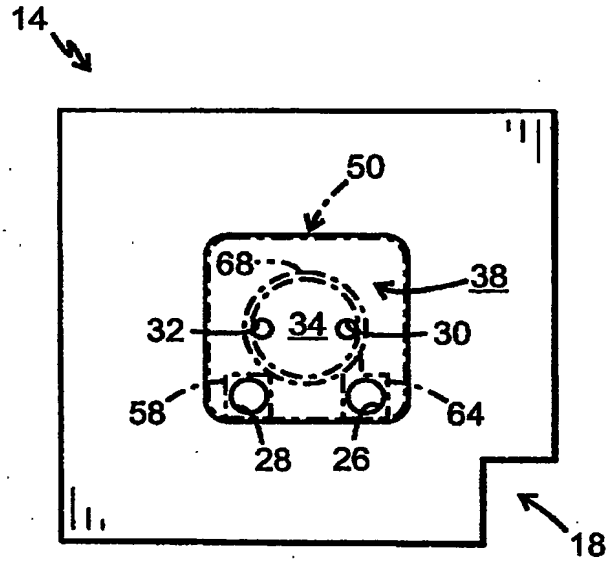


Fig. 4

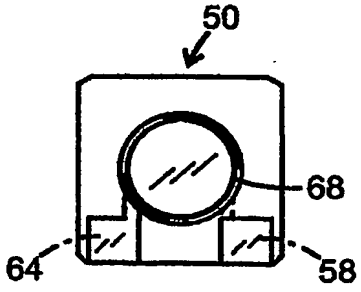


Fig. 5

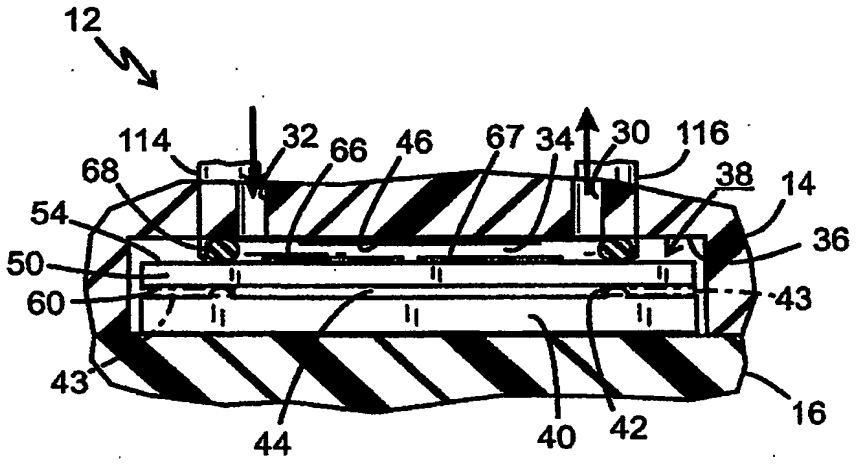

12
114
32
66
46
67
34
30
116
68
38
14
54
36
50
60
43
43
16
44
40
42

Fig. 6

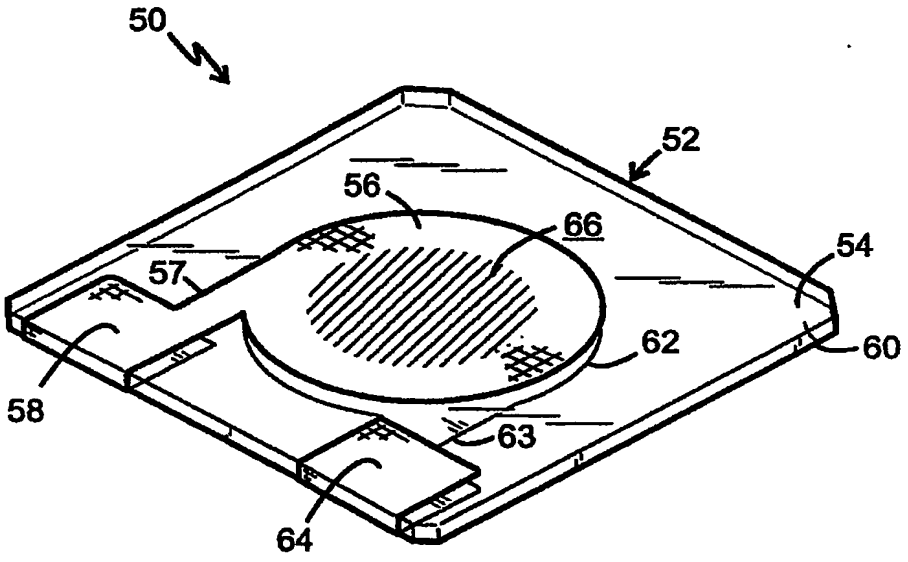

50
52
56
66
54
57
62
60
58
63
64

Fig. 7

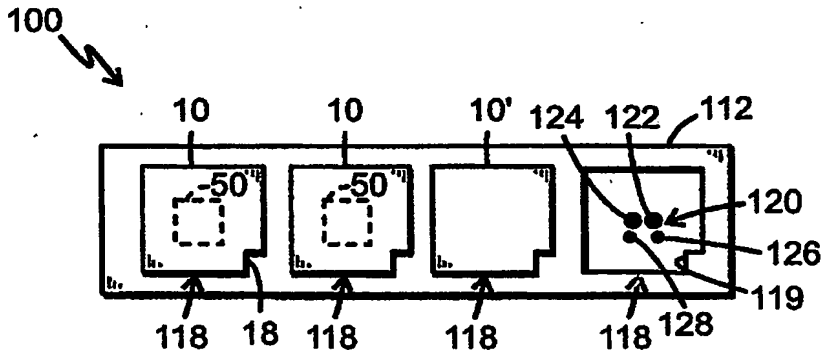

100
10
10
10'
124
122
112
50
50
120
126
119
128
118
18
118
118
118

Fig. 8

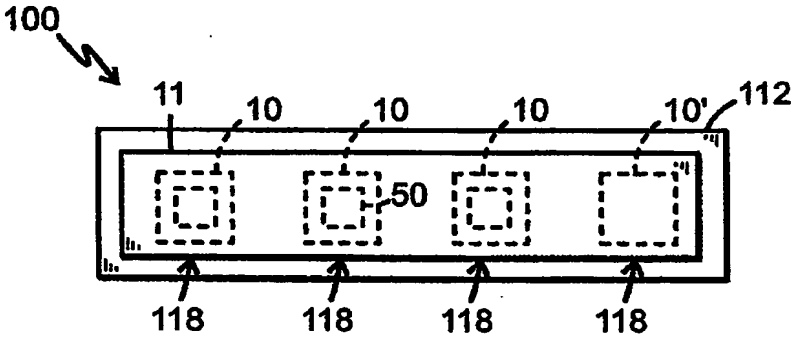

100
11
10
10
10
10'
112
50
118
118
118
118

Fig. 9

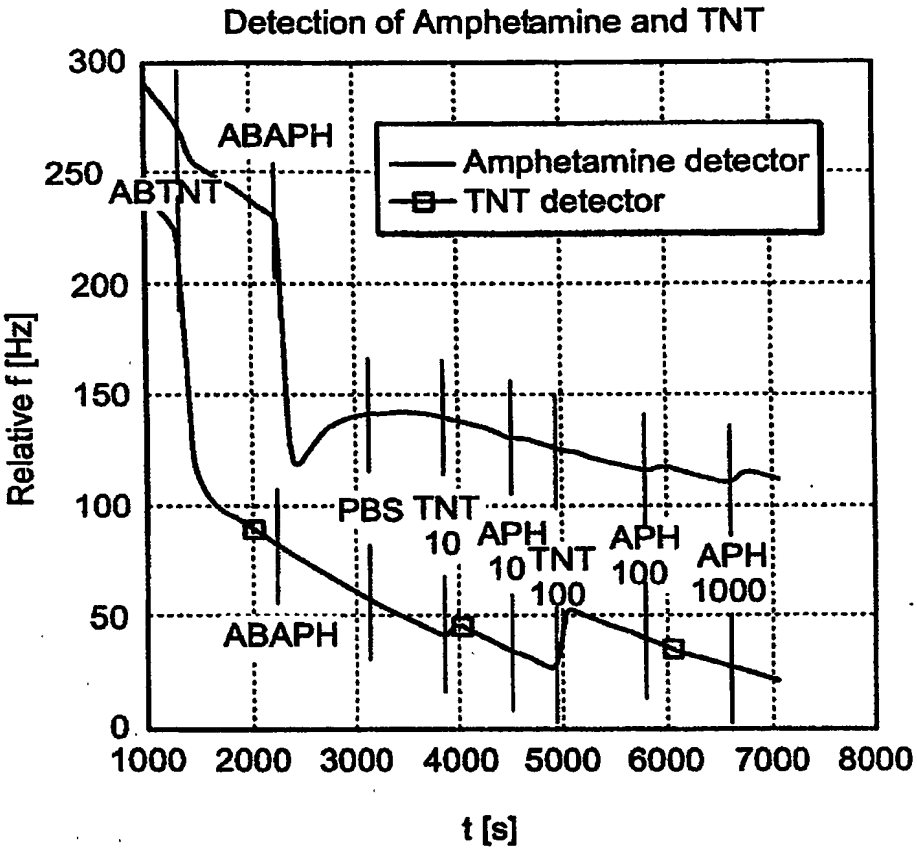
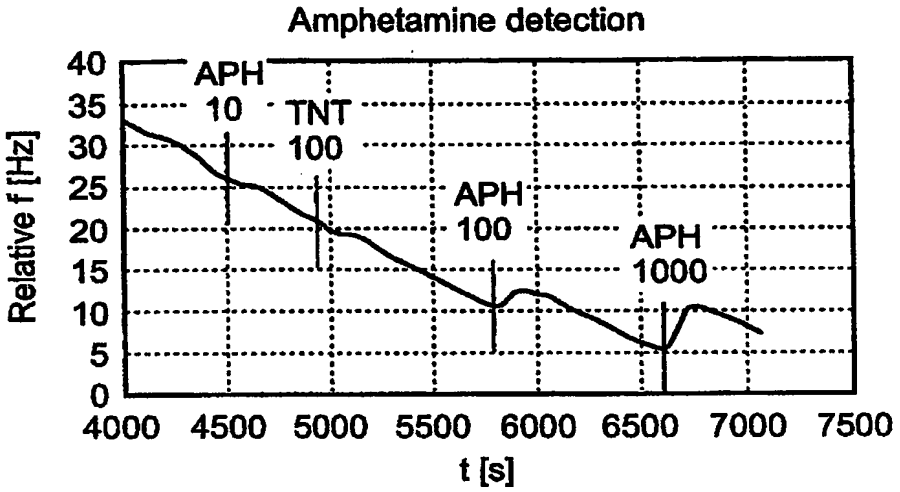

Detection of Amphetamine and TNT
Relative f [Hz]
t [s]
Amphetamine detector
TNT detector
ABAPH
ABTNT
PBS
TNT 10
APH 10
TNT 100
APH 100
APH 1000
ABAPH
300
250
200
150
100
50
0
1000
2000
3000
4000
5000
6000
7000
8000

Fig.10


Amphetamine detection
Relative f [Hz]
40
35
30
25
20
15
10
5
0
APH 10
TNT 100
APH 100
APH 1000
4000 4500 5000 5500 6000 6500 7000 7500
t [s]

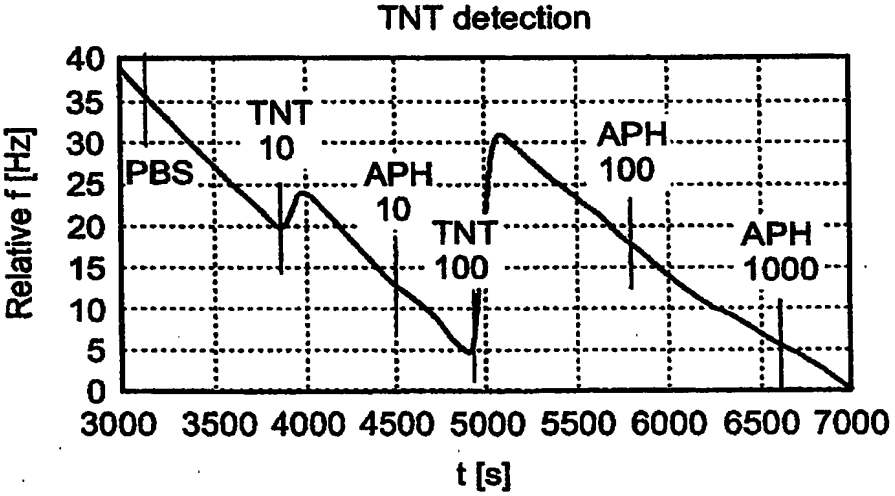

TNT detection
Relative f [Hz]
40
35
30
25
20
15
10
5
0
PBS
TNT 10
APH 10
TNT 100
APH 100
APH 1000
3000 3500 4000 4500 5000 5500 6000 6500 7000
t [s]

Fig. 11